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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/339,103	06/24/1999	CHRISTIAN KILGER	P1614-8090	2157

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EXAMINER	
HORLICK, KENNETH R	

ART UNIT	PAPER NUMBER
1637	24

DATE MAILED: 10/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/339,103	KILGER ET AL.	
	Examiner	Art Unit	
	Kenneth R Horlick	1637	

-- The MAILING DATE of this communication appears n the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-126,132-137 and 141-145* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *08/991,184* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/19/02 has been entered.

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-126, 134-137, and 143-146 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34-58 of copending Application No. 09/755,088 in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152). This is a provisional obviousness-type double patenting rejection.

The copending claims are drawn to methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other.

The copending claims do not encompass direct application of the methods/kits to RNA wherein at least one of the polymerases has reverse transcriptase activity, nor modification of said methods/kits to include a polymerase-inhibiting agent.

Gelfand et al. disclose a one-tube, one-polymerase amplification of target RNA sequences using a polymerase with reverse transcriptase activity (see, for example, the abstract).

Birch et al. disclose the advantageous use of a polymerase-inhibiting agent, including antibodies and various anhydrides, in nucleic acid amplifications (see, for example, the abstract and Fig. 1).

One of ordinary skill in the art would have been motivated to modify the methods of the copending claims by application towards RNA using a polymerase with reverse transcriptase activity, and/or application of a polymerase-inhibiting agent, because Gelfand et al. disclosed the advantages of combined reverse-transcription and amplification, and Birch et al. disclosed the benefits of using such an agent in

amplification reactions. In other words, these would have been logical, straightforward applications to achieve expected improvements. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-126, 134-137, and 143-146 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906) in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152).

These claims are drawn to methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a

higher affinity towards a chain-terminating nucleotide relative to the other, further comprising: direct application to RNA wherein at least one of the polymerases has reverse transcriptase activity; and/or use of a polymerase-inhibiting agent.

Koster et al. disclose methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other (see especially column 3, lines 25-57, column 7, lines 43-67 and column 8, lines 1-6, and Example 1 in columns 11-12).

This patent does not disclose DNA polymerase-mediated reverse transcription coupled to PCR amplification, nor the use of polymerase-inhibiting agents.

Gelfand et al. disclose a one-tube, one-polymerase amplification of target RNA sequences using a DNA polymerase with reverse transcriptase activity (see, for example, the abstract).

Birch et al. disclose the advantageous use of a polymerase-inhibiting agent, including antibodies and various anhydrides, in nucleic acid amplifications (see, for example, the abstract and Fig. 1).

One of ordinary skill in the art would have been motivated to modify the method of Koster et al. by application towards RNA using a polymerase with reverse transcriptase activity, and/or application of a polymerase-inhibiting agent, because Gelfand et al. disclosed the advantages of combined reverse-transcription and amplification, and Birch et al. disclosed the benefits of using such an agent in amplification reactions. In other words, these would have been logical, straightforward applications to achieve expected improvements. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

4. Claims 132, 133, 141, and 142 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906) in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152), and further in view of Hill (US 5,525,492).

The further limitations of these claims involve agents that lower the melting point of DNA, which is not taught in the previously-discussed references.

Hill discloses the use of a polar aprotic solvent such as DMSO in nucleic acid amplification reactions to facilitate amplification of G-C rich sequences (see column 2, lines 5-40).

One of ordinary skill in the art would have been motivated to use a melting point-lowering agent such as DMSO in the methods and kits as rejected previously because Hill taught that this advantageously provided for amplification of sequences of high G-C

content. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

5. With respect to the above rejections, the arguments of the response filed 12/06/01 have been fully considered, but are not found persuasive.

The response first argues that the method of Gelfand et al. involves a one-enzyme procedure, and thus "Gelfand et al. clearly teach against a procedure requiring more than one enzyme, such as the two different polymerases of the present claims." This is not found convincing because in the rejection, *it is the Koster et al. patent which supplies the teaching of the two-enzyme procedure; Gelfand et al. is cited for its teaching of the advantageous use of a polymerase having reverse transcription activity to carry out coupled reverse transcriptase/PCR amplification*. This benefit would have provided the motivation for using such a polymerase as one of the enzymes in the two-enzyme method of Koster et al.

Next, on pages 6-7 the response alleges unexpected results – specifically, that "[i]t was thus very surprising that the use of inhibiting agent led to clearer and more discrete bands". Also, the response mentions "more needle like peaks which are defined and easy to interpret by the reader". *However, the response fails to make any correlation between such alleged unexpected results and what is disclosed in the specification*. While it is recognized that the specification need not literally state that given results are surprising or unexpected, *there must nevertheless be basis in the specification*. If this rejection is further traversed, it is requested that it be pointed out

specifically where in the specification surprising results occur, such as where bands are described which are unexpectedly clearer and easier to interpret than those which are produced via the prior art methods.

6. In reply to the comments on page 2 of the response filed 08/19/02, it is maintained (see the Advisory action mailed 07/18/02) that the references are being argued separately, while the rejection relies on the combination of references. That is, the copending claims and Koster relate to simultaneous amplification and sequencing of nucleic acids using two different polymerases; Gelfand et al. relates to one-step transcription and amplification; Birch et al. relates to the advantageous use of polymerase-inhibiting agents; thus, it is still submitted that combination of the cited references to achieve what is being claimed would have been suggested as obtaining the combined advantages indicated in the individual references.

7. No claims are free of the prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R Horlick whose telephone number is 703-308-3905. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Kenneth R. Horlick, Ph. D.

Kenneth R Horlick
Primary Examiner
Art Unit 1637

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October 7, 2002